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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,186	11/20/2001	Qiang Liu	8325-0011.21	1799

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/990,186

Applicant(s)

LIU, QIANG

Examiner

Diana B. Johannsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0204.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. This action is responsive to the Response of May 27, 2004. Claim 1 is now pending and under consideration. Any rejections not reiterated in this action have been withdrawn. **This action is NON-FINAL.**

Election/Restriction

2. Applicant's election with traverse of QRSNLVR for F1, and QSGNLAR for F2 and F3, in the reply filed on May 27, 2004 is acknowledged.

The traversal is on the following ground(s). First, Applicant argues that "the same election of species requirement has been previously withdrawn by the Office," and that it is "inconsistent and inefficient" to reinstate the requirement. Next, Applicant refers to the text of MPEP 803.02 and argues that the Office is "improperly refusing to examine that which" Applicant regards as their invention. The response urges that the claimed invention requires the recitation of multiple sequences, as the claim is drawn to a method "of designing zinc finger proteins that recognize a target site of the form GNNGNNGNN," and that there "is no appropriate generic language that can be used to describe different species." Applicants further argue that the claim has unity of invention by virtue of having a common utility and a shared structural feature essential thereto, and that it would not be unduly burdensome for the Office to search all of the species encompassed by the claim.

These arguments have been thoroughly considered but are not persuasive. First, it is noted that a review of the election requirement of October 9, 2003 and that of May 18, 2004 reveals that they are not in fact the same requirement, as they were

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made on different grounds and had different bases. The requirement of May 18, 2004 was made because claim 1, due to the numerous structurally different sequences encompassed thereby, could not in fact be searched in its entirety without imposing a serious burden. (As evidence of this, it is noted that a search of the single elected species took weeks and generated hundreds of pages of results.) Further, as discussed in the requirement of May 18, 2004, the various sequences encompassed by the claims are sufficiently different that a reference anticipating one would not anticipate or render obvious another (thus, the claim meets the requirement for election of encompassing inventions that are sufficiently "unrelated and diverse" so as to render the instant requirement proper; Applicant is again referred to MPEP 803.02 in its entirety, which discusses instances in which an election requirement is in fact proper). With regard to Applicants' statements regarding the nature of the claimed invention, it is noted that the claim is not in fact drawn to a method of designing multiple proteins that bind to an identical target site, but rather to a method of designing a single protein that may bind to one of many thousands of different target sites (any target molecule containing three copies of the sequence NNG [either contiguously or non-contiguously], wherein N may be any of A, C, T, or G). Thus, the claim is not in fact drawn to a method limited to species with a common utility and having a common "substantial structural feature." Accordingly, Applicants' arguments are not persuasive. It is further noted that Applicants have not provided or identified any evidence showing that the numerous species encompassed by the claim are in fact obvious variants, or admitted this fact on the record.

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The requirement is still deemed proper and is therefore made **FINAL**.

It is noted that Applicants are correct that the instant election of species is for the purposes of preliminary search and examination, as discussed in MPEP 803.02 and as indicated in the requirement of May 18, 2004.

3. The species encompassed by claim 1 other than that indicated above as being elected are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on May 27, 2004.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear whether the claim requires any actual active method steps, or, alternatively, whether the claim may encompass though processes or solely mental steps that result in "designing" a protein. The claim as written merely requires several steps of "selecting," and it is not clear from the language of the claim that such steps require any actual action or manipulation on the part of a practitioner (i.e., it appears that the claim might encompass, e.g., an individual thinking about and mentally "selecting" domains so as to mentally "design" a protein).

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Accordingly, clarification is required with regard to what actual method is encompassed by the claim, such that one of skill in the art is clearly apprised of the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 1 is rejected under 35 U.S.C. 103(a) as being obvious over Eisenberg et al (U.S. Patent 6,453,242 B1 [9/17/02]) in view of Barbas (U.S. Patent 6,140,081 [10/31/00]) and Case et al (U.S. Patent 6,503,717 B2 [1/7/03]).

The applied Eisenberg et al reference has a common assignee with the instant application, and the applied Case et al reference has a common inventor and a common assignee with the instant application. Based upon the earlier effective U.S.

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filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(I)(1) and § 706.02(I)(2). It is noted that Applicant has yet to establish common ownership **at the time the invention was made**, as would be required to overcome the rejection.

Eisenberg et al teach a method for designing a zinc finger protein comprising a first (F1), a second (F2), and a third (F3) zinc finger (ordered F1, F2, F3 from N-terminus to C-terminus), which zinc finger protein binds to a target site comprising, in a 3' to 5' direction, a first (S1), a second (S2), and a third (S3) target subsite, each target subsite having the nucleotide sequence GNN, the method comprising steps of selecting the F1 zinc finger such that it binds to the S1 target subsite, selecting the F2 zinc finger

such that it binds to the S2 target subsite, and selecting the F3 zinc finger such that it binds to the S3 target subsite, thereby designing a zinc finger protein that binds to a target site (see entire reference particularly Figure 2, Example 6, and Column 20, line 25 to Column 22, line 42).

Eisenberg et al do not teach a method comprising selecting the F1 zinc finger such that it binds to the S1 target subsite, wherein if S1 comprises GAA, F1 comprises the amino acid sequence QRSNLVR, as required by the claim. Additionally, Eisenberg et al do not teach a method comprising selecting the F2 and F3 zinc fingers such that they bind to S2 and S3 target subsites, wherein if S2 and S3 comprise GAA, F2 and F3 comprise the amino acid sequence QSGNLAR.

Barbas teaches that a zinc finger domain having the amino acid sequence QRSNLVR has binding specificity for a target subsite comprising GAA (see entire reference, particularly Figure 1A).

Case et al teach that a zinc finger domain having the amino acid sequence QSGNLAR has binding specificity for a target subsite comprising GAA (see entire reference, particularly Example 1, Table 1).

In view of the teachings of Barbas and Case et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Eisenberg et al so as to have included therein steps of selected the amino acid sequences QRSNLVR and/or QSGNLAR for binding to target subsites comprising GAA, and thereby to have designed a zinc finger protein meeting the requirements of the claim (as well as additional species of zinc finger proteins

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comprising these sequences in a different order and/or in different combinations).

Given the teachings of Barbas and Case et al that these particular amino acid sequences specifically bind to GAA target sequences, an ordinary artisan would have been motivated to have made such a modification for the advantage of designing a zinc finger protein or zinc finger proteins having the capability of specifically binding to this nucleotide sequence in any target molecules of interest that contain it. Further, an ordinary artisan would have been motivated to have designed and prepared the particular species of the instant claim (as well as the additional variants/species referenced above) for the advantage of having available particular zinc finger proteins specific for GAA target sequences for use in screening methods, optimization of binding to achieve expression of particular GAA-containing target genes under particular conditions, etc.

9. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eisenberg et al (WO 00/42219 A1 [7/20/00]) in view of Barbas (U.S. Patent 6,140,081 [10/31/00]) and Case et al (WO 01/40798 A2 [6/7/01; filed 12/6/00]).

It is noted that effective filing date of the instant application is November 20, 2001, and that the Case et al reference therefore qualifies as prior art under both 35 USC 102(e) and 35 USC 102(a). The Eisenberg et al and Barbas et al references are prior art under 35 USC 102(b).

Eisenberg et al teach a method for designing a zinc finger protein comprising a first (F1), a second (F2), and a third (F3) zinc finger (ordered F1, F2, F3 from N-terminus to C-terminus), which zinc finger protein binds to a target site comprising, in a

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3' to 5' direction, a first (S1), a second (S2), and a third (S3) target subsite, each target subsite having the nucleotide sequence GNN, the method comprising steps of selecting the F1 zinc finger such that it binds to the S1 target subsite, selecting the F2 zinc finger such that it binds to the S2 target subsite, and selecting the F3 zinc finger such that it binds to the S3 target subsite, thereby designing a zinc finger protein that binds to a target site (see entire reference particularly Figure 2, Example 6, and pages 29-33).

Eisenberg et al do not teach a method comprising selecting the F1 zinc finger such that it binds to the S1 target subsite, wherein if S1 comprises GAA, F1 comprises the amino acid sequence QRSNLVR, as required by the claim. Additionally, Eisenberg et al do not teach a method comprising selecting the F2 and F3 zinc fingers such that they bind to S2 and S3 target subsites, wherein if S2 and S3 comprise GAA, F2 and F3 comprise the amino acid sequence QSGNLAR.

Barbas teaches that a zinc finger domain having the amino acid sequence QRSNLVR has binding specificity for a target subsite comprising GAA (see entire reference, particularly Figure 1A).

Case et al teach that a zinc finger domain having the amino acid sequence QSGNLAR has binding specificity for a target subsite comprising GAA (see entire reference, particularly Example 1, Table 1).

In view of the teachings of Barbas and Case et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Eisenberg et al so as to have included therein steps of selected the amino acid sequences QRSNLVR and/or QSGNLAR for binding to target subsites

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comprising GAA, and thereby to have designed a zinc finger protein meeting the requirements of the claim (as well as additional species of zinc finger proteins comprising these sequences in a different order and/or in different combinations). Given the teachings of Barbas and Case et al that these particular amino acid sequences specifically bind to GAA target sequences, an ordinary artisan would have been motivated to have made such a modification for the advantage of designing a zinc finger protein or zinc finger proteins having the capability of specifically binding to this nucleotide sequence in any target molecules of interest that contain it. Further, an ordinary artisan would have been motivated to have designed and prepared the particular species of the instant claim (as well as the additional variants/species referenced above) for the advantage of having available particular zinc finger proteins specific for GAA target sequences for use in screening methods, optimization of binding to achieve expression of particular GAA-containing target genes under particular conditions, etc.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Diana B. Johannsen", with a long horizontal flourish extending to the right.

Diana B. Johannsen
Primary Examiner
November 2, 2004